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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,384	11/15/2001	Avi J. Ashkenazi	P2730P1C35	4942

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EXAMINER

ROMEO, DAVID S

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/997,384

Applicant(s)

ASHKENAZI ET AL.

Examiner

David S. Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 119-126 and 129-136 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 119-126 and 129-136 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>0105,1204</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed 12/10/2004 has been entered. Claims 119-126, 129-136 are pending and being examined.

5

Priority

According the preliminary amendment filed 09/03/2002 this application is a CON of 09/941,992, filed 08/28/2001, which claims the benefit of 60/213,637, filed 06/23/2000. The benefit claim to 60/213,637, filed 06/23/2000, is not proper because 09/941,992 was not filed within twelve months from the filing date of the provisional application.

10

Appropriate correction is required.

New Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

15 Claims 132-136 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing angiogenesis in adrenal cortical epithelial cells, does not reasonably provide enablement for stimulating endothelial cell proliferation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

20

The claims are directed to or encompass stimulating endothelial cell proliferation with a genus of polypeptides having a recited % identity to SEQ ID NO: 371. Thus the present claims

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are directed to stimulating the proliferation of all conceivable endothelial cells with claimed genus of polypeptides. The present specification discloses:

Example 149

5 [4396] Stimulation of Endothelial Cell Proliferation (Assay 8)

10 [4397] This assay is designed to determine whether PRO polypeptides of the present invention show the ability to stimulate adrenal cortical capillary endothelial cell (ACE) growth. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

15 No other examples of stimulating endothelial cell proliferation with the PRO1186 polypeptide are provided. The examiner is aware that the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. Lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and
20 undeveloped art.

There is a lack of predictability in the art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See
Bowie (U) page 1306, column 1, full paragraph 1, or Ngo (V) page 433, full paragraph 1, and
25 page 492, full paragraph 2.

In addition, LeCouter (W) identifies a EG-VEGF polypeptide that is identical SEQ ID NO: 371 of the present invention (page 878, Figure 1). EG-VEGF is selective for endocrine

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gland endothelium (Title and Abstract). See also Ferrara (B) (U.S. Provisional application No. 20020172678), page 2, paragraph 0011.

The skilled artisan is left to an unduly extensive amount of experimentation wherein a polypeptide comprising the amino acid sequence of SEQ ID NO: 371 is randomly mutated and through trial and error experimentation is left to determine how to induce stimulate endothelial cell proliferation in tissues that have been shown to be non-responsive to this factor. The specification lacks guidance for stimulating endothelial cell proliferation in non-responsive endothelial cells.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 119-123 are rejected under 35 U.S.C. 102(e) as being anticipated by Sheppard (A) (U. S. Patent No. 6,485,938).

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The claims are directed to or encompass a genus of polypeptides that induce chondrocyte redifferentiation. This activity was first disclosed in PCT/US00/08439, 03/30/2000.

Accordingly, reciting this limitation destroys Applicants' benefit of the filing dates of the earlier filed applications.

5 Sheppard discloses an isolated Zven2 polypeptide (paragraph bridging columns 3-4) that is identical to the present application's SEQ ID NO: 371, as indicated below (Qy = SEQ ID NO: 371) (Db = Zven2):

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: May 6, 2004, 12:48:28 ; Search time 22 Seconds
(without alignments)
246.397 Million cell updates/sec

Title: US-09-997-384-371
Perfect score: 589
Sequence: 1 MRGATRVSIMLLLVTVSDCA.....CSRFPDGRYRCMDLKNINF 105

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 200 summaries

Database : Issued Patents_AA:*
1: /cgn2_6/ptodata/2/iaa/5A_COMB.pep:*
2: /cgn2_6/ptodata/2/iaa/5B_COMB.pep:*
3: /cgn2_6/ptodata/2/iaa/6A_COMB.pep:*
4: /cgn2_6/ptodata/2/iaa/6B_COMB.pep:*
5: /cgn2_6/ptodata/2/iaa/PCTUS_COMB.pep:*
6: /cgn2_6/ptodata/2/iaa/backfiles1.pep:*

US-09-712-529-5
; Sequence 5, Application US/09712529
; Patent No. 6485938
; SEQ ID NO 5
; LENGTH: 105
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-712-529-5

Query Match 100.0%; Score 589; DB 4; Length 105;
Best Local Similarity 100.0%; Pred. No. 6.8e-59;
Matches 105; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEEC 60

Db 1 MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEEC 60

Qy 61 HPGSHKVPFFRRKRKHTCPCLPNLLCSRFPDGRYRCMDLKNINF 105

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db 61 HPGSHKVPFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF 105.

Zven2 was first disclosed in U.S. Provisional application No. 60/165,905, filed Nov. 16,

5 1999.

Double Patenting

10 The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

15 A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

20 Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 119-124, 126, 130-136 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of
25 copending Application No. 10/692,299. Although the conflicting claims are not identical, they are not patentably distinct from each other because SEQ ID NO: 371 or the present application is identical to SEQ ID NO: 2 of the copending application. Both sets of claims are directed to or encompass the same polypeptide or polypeptides having overlapping per cent identities to the same polypeptide. A fusion protein comprising epitope tag or an Fc region of an
30 immunoglobulin, as presently claimed, is an obvious variant of the polypeptide of the copending claims.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 125, 129 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 8 of copending Application No. 10/692,299. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300. CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890. ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.


DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647